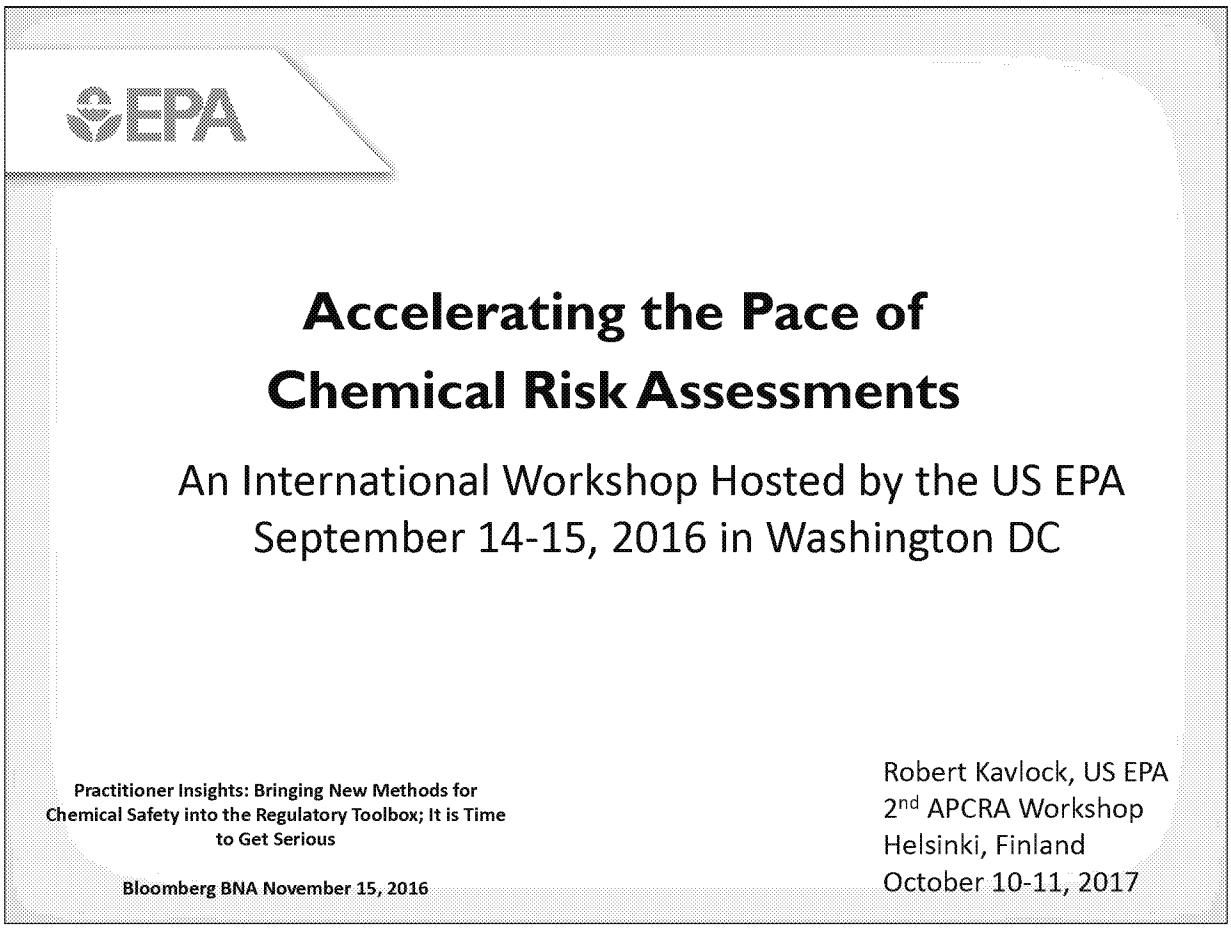
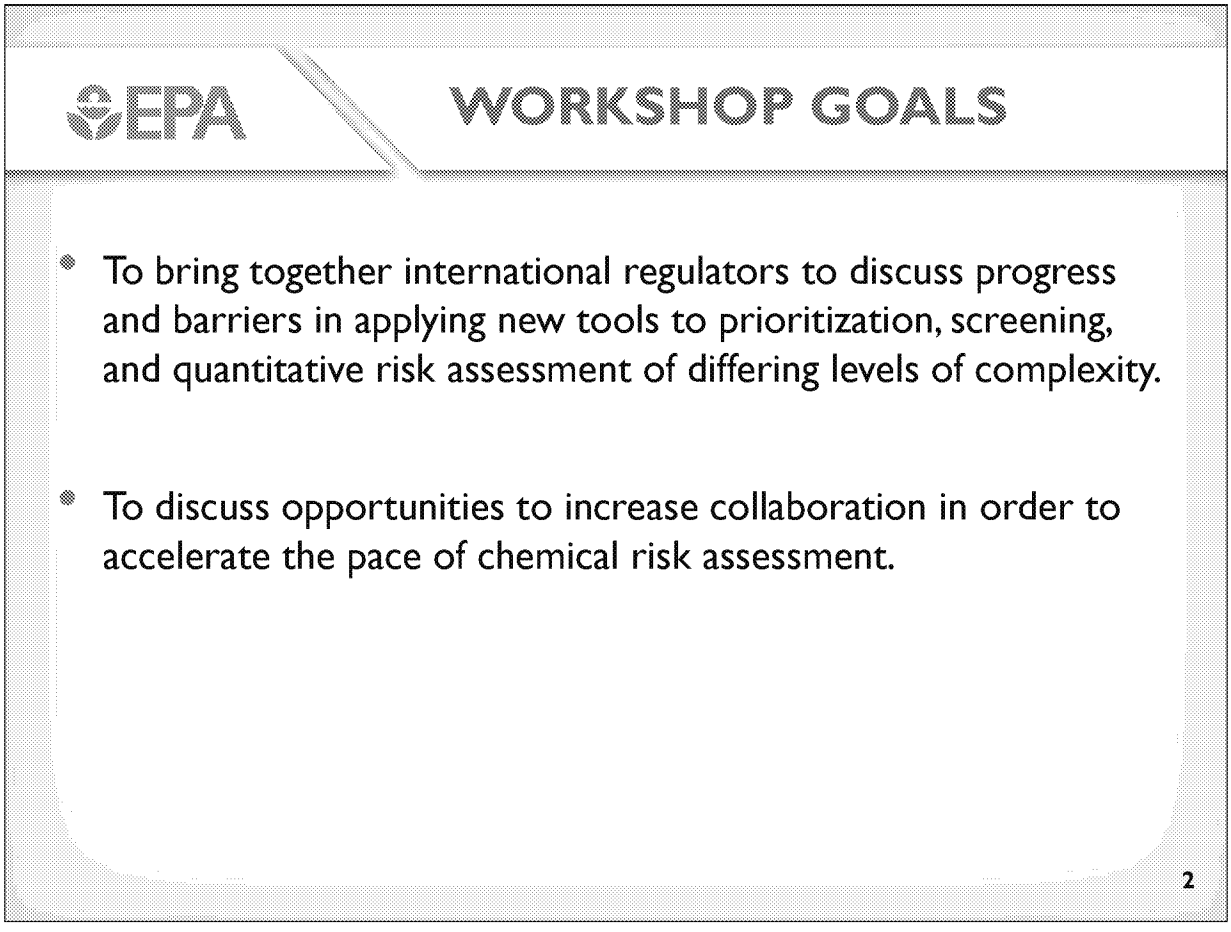


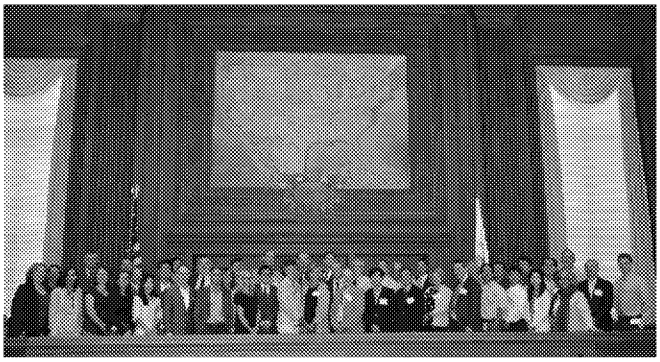

Accelerating the Pace of Chemical Risk Assessments workshop, September 14-15, 2016




# Ex. 5 Deliberative Process (DP)

EPA

# Participants



- **United States:** EPA, California EPA, NTP, CPSC
- **Canada:** Health Canada
- **Europe:** EChA, EFSA, JRC, OECD, INERIS, RIVM
- **Asia:** Korea – Ministry of the Environment, Japan – Ministry of the Environment & Ministry of Health, Welfare and Labour, Singapore – A*STAR, Taiwan – SAHTECH
- **Australia:** NICNAS



EChA – European Chemicals Agency
EFSA – European Food Safety Authority
JRC – Joint Research Centre
OECD – Organisation for Economic Cooperation and Development
RIVM – National Institute for Public Health and the Environment
A*STAR – Agency for Science Technology and Research
SAHTECH – The Safety and Health Technology Center
NICNAS – National Industrial Chemicals Notification and Assessment Scheme

# Desired Outcomes

- Compilation of a master list of chemicals of common international interest for ongoing and future NAM application
- Identification of potential sources of NAM information and how such information could be shared and exploited
- Common understanding of current state of the science applications of New Approach Methods (NAMs), including the regulatory context and presentation of practical examples
- **Commitment to development and sharing of case studies of mutual interest**

# Barriers to Acceptance

- **The Use of Laboratory Animal Studies As the Ultimate Gold Standard**
  - Limited coverage of some emerging health issues in the human population
  - Lack of concordance with evidence accumulating in population studies
- **Potential Limitations of Existing Technologies**
  - Metabolic capabilities, lack of more systems level models
- **Benchmarking NAMs Against Laboratory Animal Studies**
  - Unlikely to encounter one-to-one replacements
- **Lack of Understanding and Confidence in Applying NAMs**
  - Note success with emergency responses and with the US EPA EDSP
- **Differing Regulatory Needs for Decision Making, with Some Requiring Specific Testing Requirements**
- **Current Inability to Share Information Across National Boundaries**

## Action Items

- **Foundational –** must be conducted first to take advantage of other activities.
  - Data Platforms: For chemicals of common interest, hazard data repositories. √
  - Classification Systems for NAMS: There are systems for traditional toxicity data but not for NAMs.
- **Experimental**
  - Case Studies: It is necessary to explore how to make NAM case studies useful to regulators. √ √ √
  - Data Generation: As we consider case studies, we need to also think about generating data that will help them achieve success. √



# Ex. 5 Deliberative Process (DP)

## Proposed Case Studies

1. Outline for a project proposal to assess chemicals, using and developing New Approach Methodologies (NAMs) – ECHA
   - Partners: Health Canada, EPA, JRC, EC, RIVM, EFSA, A*STAR
   - assess chemicals with very limited toxicological data and significant potential exposure, using both classical toxicological studies and NAM data to use and inform the further development needs for NAM
2. Revisiting and Updating Chemical Categorizations with NAMs – US EPA and Health Canada
   - Partners: ECCC (Environment and Climate Change Canada)
   - develop the machinery to cluster and categorize chemicals based on the available bioactivity data and structural information represented in available in vitro assays.
3. Examining the Utility of In Vitro Bioactivity as a Conservative Point of Departure: A Case Study – US EPA and Health Canada
   - Partners: EChA, EFSA, A*STAR
   - elucidate whether a "region of safety" (ROS), i.e. a threshold below which no bioactivity or toxicity would be anticipated, can be identified using NAMs for a list of chemicals with existing human health evaluations.

7

**Ex. 5 Deliberative Process (DP)**

# Ex. 5 Deliberative Process (DP)

## Proposed Case Studies (cont'd)

4. Triaging Exposure Data and Modeling Needs for Exogenous Chemicals – US EPA
   - Partners: HealthCanada
   - evaluate the landscape of different levels of information required for generating defensible exposure predictions for use in RA for a set of case study chemicals.
5. Linking Exposure to Toxicology Using Lead as Case Study – US EPA
   - Partners: EFSA, CalEPA
   - advancing the science and pace of multimedia chemical risk assessments using higher-tier exposure models and biomonitoring information through two data-rich case studies: aggregate multipathway lead exposures and PFOS/PFOA exposures.
6. NAMs for Assessing Endocrine Disrupting Properties - INERIS
   - Partners: OECD, Health Canada, EPA, ECVAM
   - build up a database on New Approach Methods (NAMs) that can be actually applied for assessing endocrine disrupting properties of substances or mixtures in environmental samples.



# Ex. 5 Deliberative Process (DP)

# Ex. 5 Deliberative Process (DP)

## Proposed Case Studies (cont'd)

7. Application of NAMs to Chemical Category for Class of Perfluoroalkylated Substances – US EPA
   - Partners: EFSA, HealthCanada, NTP
   - develop quantitative, health-based toxicity information, including classical toxicity values where appropriate, to inform decisions regarding public health of PFAS compounds.
8. Developing an in vitro amphibian skin model for testing chemical: A conceptual proposal – EFSA
   - develop a conceptual proposal for future use of an *in vitro* amphibian skin model as well as the development of toxicokinetic models to investigate the contribution of the skin to the systemic exposure in amphibians in comparison to birds and mammals.
9. Developing tentative reference doses (tRfDs) based on key in vitro assays for endocrine disrupting chemicals (EDCs)- Seoul National University
   - develop an approach to derive tentative RfD (tRfD) for new EDCs based on well characterized endocrine modes of action using a series of in vitro screening assays.

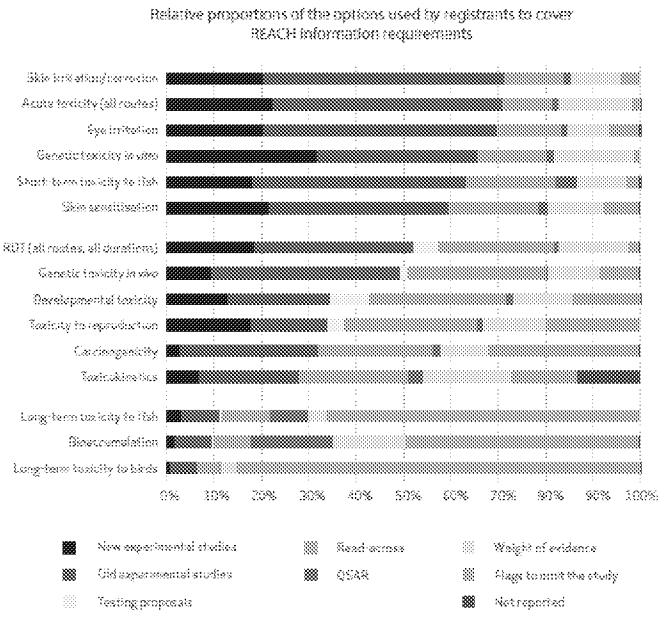


**Ex. 5 Deliberative Process (DP)**

# Ex. 5 Deliberative Process (DP)

## Post-Workshop Events

- Executive Summary from the workshop finalized (November 2016).
- Regular teleconferences continue to discuss case studies and collaborative efforts.
- Ongoing discussions between EChA, OECD and JRC on concept of eChem Portal as data repository.
- ~~OECD EAGMST discussion on value of classification systems for NAMs.~~
- Follow-up meeting to be hosted by EChA on 10-11 October 2017 in Helsinki to focus on case studies and next steps.


Relative proportions of the options used by registrants to cover REACH information requirements
Skin irritation/corrosion
Acute toxicity (all routes)
Eye irritation
Genetic toxicity in vitro
Short-term toxicity to fish
Skin sensitisation
RDT (all routes, all durations)
Genetic toxicity in vivo
Developmental toxicity
Toxicity to reproduction
Carcinogenicity
Toxicokinetics
Long-term toxicity to fish
Bioaccumulation
Long-term toxicity to birds
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
New experimental studies
Old experimental studies
Testing proposals
Read-across
QSAR
Waiver
Weight of evidence
Flags to omit the study
Not reported

## Desired Outcomes

- Opportunity for case study members to have a face to face discussions
- Understanding of what case studies have done and how they support the objectives of APCRA
- Exploration of gaps in the overall effort
- Articulation of organizational commitments and timelines for progress
- Discussion on communication and sustainability of APCRA